

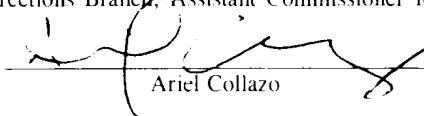
C3016 Receipt

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Robert I. Garver et al. :
Appln. No. 09/359,593 : Art Unit: 1652
Filed: July 23, 1999 : Examiner: TO BE ASSIGNED
For: CONTROLLED RELEASE OF BIOACTIVE : Atty Docket: JHV-009.01
SUBSTANCES :

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, in an envelope addressed to Customer Corrections Branch, Assistant Commissioner for Patents, Washington, D.C. 20231 on September 27, 1999.



Ariel Collazo

REQUEST FOR CORRECTION OF FILING RECEIPT

Customer Corrections Branch
Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Enclosed is a copy of the Filing Receipt for the above-referenced application.

Please correct the title of the invention from "CONTROLLED DELIVERY OF BIOACTIVE SUBSTANCES" to --**CONTROLLED RELEASE OF BIOACTIVE SUBSTANCES**-- as originally submitted on the first page of the specification (copy attached).

Please insert the residences of the inventors as follows:

Robert I. Garver - Hoover, AL;

Subramanian Kalyanasundaram - Gaithersburg, MD;

Kam W. Leong - Ellicott City, MD

Please correct the spelling of inventor "Subramanin" to --**Subramanian**-- and insert the middle initial "W." to the name of "**Kam W. Leong**--.

Should there be any questions concerning this request, please contact the undersigned at (617) 832-1169.

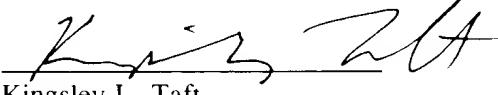
Respectfully submitted,

FOLEY, HOAG & ELIOT LLP

September 27, 1999

Date

Patent Group
Foley, Hoag & Eliot LLP
One Post Office Square
Boston, MA 02109-2170
Tel. (617) 832-1000



Kingsley L. Taft
Reg. No. 43,946

FILING RECEIPT



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTORNEY DOCKET NO.	DRWGS	TOT CL	IND CL
09/359,593	07/23/99	1652	\$0.00	JHV-009.01	0	48	9

FOLEY HOAG & ELIOT LLP
ONE POST OFFICE SQUARE
BOSTON MA 02109-2170



Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts of Application" ("Missing Parts Notice") in this application, please submit any corrections to this Filing Receipt with your reply to the "Missing Parts Notice." When the PTO processes the reply to the "Missing Parts Notice," the PTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s) ROBERT I GARVER, RESIDENCE NOT PROVIDED; SUBRAMANIN KALYANASUNDARAM, RESIDENCE NOT PROVIDED; KAM LEONG, RESIDENCE NOT PROVIDED.

CONTINUING DATA AS CLAIMED BY APPLICANT—
PROVISIONAL APPLICATION NO. 60/093,946 07/23/98

IF REQUIRED, FOREIGN FILING LICENSE GRANTED 08/31/99
TITLE
CONTROLLED DELIVERY OF BIOACTIVE SUBSTANCES

PRELIMINARY CLASS: 435

RECEIVED

SEP 03 1999

FOLEY HOAG & ELIOT LLP
PATENT DEPT.

DATA ENTRY BY: HINES, BRENDA

TEAM: 06 DATE: 08/31/99



LICEN~~S~~E FOR FOREIGN FILING UNDER
Title 35, United States Code, Section 1
Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "FOREIGN FILING LICENSE GRANTED" followed by a date appears on the reverse side of this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.11. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related application(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations, especially with respect to certain countries, of other agencies; particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR Parts 121-128)); the Office of Export Administration, Department of Commerce (15 CFR 370.10 (j)); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "FOREIGN FILING LICENSE GRANTED" DOES NOT appear on the reverse side of this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

PLEASE NOTE ---- The Following Information about the Filing Receipt:

The articles such as "a," "an" and "the" are not included as the first words in the title of an application. They are considered to be unnecessary to the understanding of the title.

The words "new," "improved," "improvement," "improvements in or relating to" are not included as the first words in the title of an application because a patent application is, by nature, a new idea or improvement.

The title may be truncated if it consists of more than 4 lines of 70 characters each (letters and spaces combined).

The inventor information may be truncated if the family name consists of more than 25 characters (letters and spaces combined) and if the given name consists of more than 25 characters (letters and spaces combined). The inventor's residence allows for up to 40 characters (letters and spaces combined).

The docket number allows a maximum of 12 characters.

If your application was submitted under 37 CFR 1.10, your filing date should be the "date in" found on the Express Mail label. If there is a discrepancy, you should submit a request for a corrected Filing Receipt along with a copy of the Express Mail label showing the "date in."

Customer Address may have been modified to conform to U.S. Postal rules.

Please direct correction, including a copy of your Filing Receipt, to:

Assistant Commissioner for Patents
Office of Initial Patent Examination
Customer Service Center
Washington, DC 20231

Controlled Release of Bioactive Substances

Related Application Information

This Application claims the benefit of priority under 35 U.S.C. § 119(e) to
5 Provisional Application 60/093,946, filed July 23, 1998, the specification of which is
incorporated by reference in its entirety.

Acknowledgment of Government Rights

The present invention was made in part with support from the U.S. Government under
10 a grant from the National Institutes of Health. The U.S. Government has certain rights in this
invention.

Introduction

The effectiveness of gene therapy is limited in part by the delivery systems used to administer the gene of interest. In general, gene therapy involves the transfer of genetic material into the cells of a patient to provide expression of delivered genes. However, the development of clinical applications of gene therapy has been limited by, among other things, inefficient gene transfer, transient expression, immune rejection, and cytotoxicity. Such a result is not entirely unexpected, because many of the steps required for gene therapy, including cell membrane penetration, intracellular trafficking and nuclear entry of genes, are incompletely understood.

One means of addressing some of these issues involves the use of recombinant viruses. However, the therapeutic utility of recombinant viruses, in particular of adenoviruses, is limited in part by difficulties in directing the viruses to specific sites, and by the requirement for bolus administration, both of which limit the efficiency of target tissue infection. Recombinant adenovirus has emerged as a leading vector for the delivery of new genes to mammalian cells. Advantages include the extensive understanding of the virus biology, well-established methods for the generation of high titer recombinant adenoviruses, and generally high expression of the viral transgene, among others (Curiel et al., *Gene Therapy for Diseases of the Lung* 104:29-52). Two important limitations of the existent